

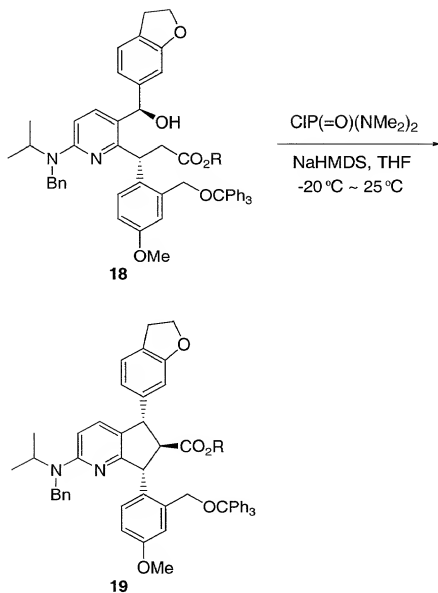
Table 5: The Effect of Solvent on Grignard Addition of (17)  
(R is isopropyl)

Solvent	THF	NMP	NEP	(1:1) NMP/THF
T (°C )	-78	-20 to -10	-50 to 25	-40 to -50
Selectivity	3.8/1	22/1	NR	35/1

- 5 As shown in Table 5, the selectivity of the Grignard addition to aldehyde compound (17) where R is isopropyl, in THF is very low (3.8/1). In NMP, the selectivity improves to about 22/1 at a temperature about -20°C to about -10°C, but large amounts of a side product is observed. A mixed solvent of (1:1) NMP:THF at a temperature of about -40°C to about -50°C significantly enhances the selectivity
- 10 resulting a cleaner reaction with a higher stereoselectivity (35/1).

REACTION SCHEME F

## Cyclization



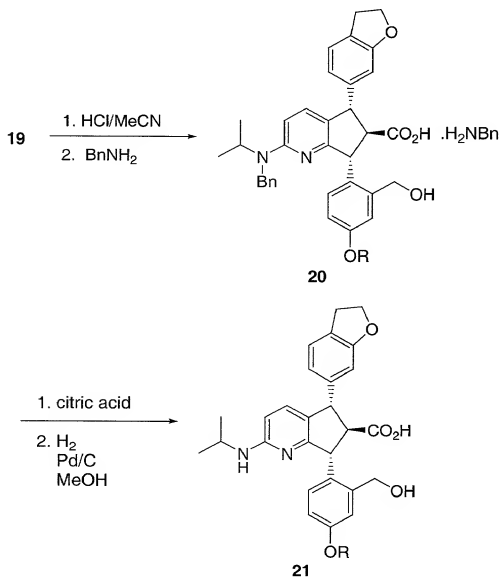
5    R = (C<sub>1</sub>-C<sub>6</sub>)-alkyl

10    In Reaction Scheme F, cyclization of a Grignard addition compound (18) by treatment with about 1 to 2 equivalents of N,N,N',N'-tetramethylphosphorodiamidic chloride, [(CH<sub>3</sub>)<sub>2</sub>N]<sub>2</sub>POCl, and about 1 to 6 equivalents (preferably 4 to 5 equivalents) of sodium hexamethyldisilazide (NaHMDS) or LiHMDS in an aprotic solvent at about -80°C to about 30°C

(preferably about -20°C to about 25°C) affords a cyclized compound (19). Preferred aprotic solvents are THF, toluene and a mixture of THF/toluene. A reaction in NaHMDS and THF are preferred.

5 REACTION SCHEME G:

Deprotection-Hydrogenolysis



R = H or (C<sub>1</sub>-C<sub>6</sub>)-alkyl